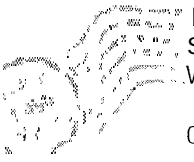
201-14411



NCIC HPV
Sent by: Mary-Beth Weaver

04/17/2003 09:27 AM

To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Environmental Defense comments on Mononitriles Category

Richard_Denison@environmentaldefense.org on 04/16/2003 04:09:57 PM

To: oppt.ncic@epamail.epa.gov, hpv.chemrtk@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA, Karen Boswell/DC/USEPA/US@EPA, Edwin.L.Mongan-1 @usa.dupont.com
cc: lucierg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org

Subject: Environmental Defense comments on Mononitriles Category

(Submitted via Internet 4/16/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and Edwin.L.Mongan-1@usa.dupont.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for the Mononitriles Category.

This test plan was prepared by Dupont and is well-written and informative. It covers four chemicals: 2-methyl-3-butenenitrile (16529-56-9), 2-pentenenitrile (25899-50-7, cis isomer; 26294-98-4, trans isomer; and 13284-42-9, both isomers), 3-pentenenitrile (4635-87-4, both cis and trans isomers) and 4-pentenenitrile (592-51-8). Mononitriles arise during the synthesis of adiponitrile and may be considered impurities, by-products, -process streams or desired products of commercial value (i.e. 3-pentenenitrile). Those that are desired products and impurities are entirely consumed on-site, whereas portions of those that are byproducts and process streams are sold for use as chemical intermediates, according to the sponsor.

While we agree that the proposal for a category is scientifically justified, we do not agree with all parts of the proposed test plan. Specifically, we recommend that two members of the proposed category should be tested for repeat dose/reproductive/developmental toxicity and for chromosomal aberrations, rather than just one of the members as proposed by the sponsor. Specific comments are as follows:

1. Available data for biodegradation and aquatic toxicity indicate that 4-pentenenitrile has somewhat different biological and/or physiochemical properties than the other three proposed category members; it degrades quickly in the environment, whereas the other members are quite resistant to biohegradation. This finding raises the possibility that 4-pentenenitrile forms metabolites not formed by the other members. Since metabolism data is not provided in the test plan, there remains a reasonable possibility that the metabolites and/or degradation products possess biological activities different than those of the parent compounds. For this reason, we recommend that 4-pentenenitrile be tested along with 2-pentenenitrile in cases where data for specific endpoints are not available.

2. The revised test plan includes both the cis and trans isomers of 2-pentenenitrile. What is the isomeric composition of the commercially available material and what will be the composition of the actual test substance to be used in the additional studies proposed by the sponsor?

3. We commend the sponsor for providing an objective evaluation of the adequacy of available data. The sponsor proposes using 2-pentenenitrile as the prototypical member of the category for further studies, including a combined reproductive/developmental/repeat dose study and an in vitro chromosomal aberration study. We agree with the selection of 2-pentenenitrile, but we also recommend that the sponsor conduct a combined study using 4-pentenenitrile as a test substance for the reasons given in point 1. Separate studies on these two members of the proposed category will provide data which likely spans the range of biological activities for the entire mononitrile category, and hence will provide a reasonable scientific basis for extrapolating to other members of the class.

4. The rationale for the proposed mononitrile category would be more convincing if gene expression data were available to demonstrate that all members of the proposed category caused the same pattern of gene expression changes in an in vitro or in vivo system. For example, if all four proposed members elicited a common pattern of gene expression changes, then we would agree that the proposed 2-pentenenitrile studies would be adequate to fulfill HPV requirements.

5. We agree with the sponsor that available data for ecological endpoints is sufficient to fulfill requirements of the HPV program.

6. The test plan includes data on worker exposure and safety practices. While not explicitly required by the HPV program, this kind of information is helpful and consistent with the spirit of "Right to Know Initiatives". We do note, however, that the AEL recommended by Dupont for workers is 0.3 ppm. Since the apparent NOEL is 0.3 ppm or less, we urge Dupont to reconsider its recommended AEL and enforce a lower exposure level in the workplace. In particular, we note that the exposure levels for 2-pentenenitrile experienced by ADN Production Operators were reported as high as 0.79 ppm. Other plants and other exposure situations do not appear to pose a health risk, based on the descriptions provided by the sponsor.

7. If Dupont proposes to place all of these mononitriles into a single category for hazard assessment purposes under the HPV program, then for purposes of risk assessment and worker safety evaluations, exposures to all proposed members should be aggregated.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
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